Editorial Review

Environmental stress, adaptation and evolution: an overview

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Environmental stress can be characterized as a force shaping adaptation and evolution in changing environments, and it is a property of both the stressor and the stressed. Here we aim to give an overview of the state of the art of evolutionarily orientated stress research and the progress it has made during the last decade. We do this by introducing the contributions to this issue of the Journal of Evolutionary Biology that resulted from a workshop held in August 2004 in Sandbjerg (Denmark), sponsored by the European Society of Evolutionary Biology (ESEB).

Introduction

> Naturalists continually refer to external conditions, such as climate, food &c., as the only possible cause of variation. In one limited sense, as we shall hereafter see, this may be true; but is it preposterous to attribute to mere external conditions, the structure, for instance, of the woodpecker, with its feet, tail, beak, and tongue, so admirably adapted to catch insects under the bark of trees.
>
> (Darwin, 1875)

The statement above by Darwin can already be found on the second page of the introductory chapter of his *On the Origin of Species by Means of Natural Selection* and expresses his view that, even though adaptation of individuals to their natural physical and biotic environment is central in his theory of evolution, he thought that this was mainly governed through intra and inter-specific competition. To Darwin, competition between 'organic beings' was far more significant than adaptation to environmental conditions. This preponderance of competition in his theory is expressed even more clearly in Chapter III of the book. Based on the observation that many organisms produce far more offspring than necessary to sustain their numbers, he describes his basic idea

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concerning the 'struggle for existence' that forms the foundation of his theory of evolution and states that numbers are not so much limited by lack of adaptation to particular climates but much more by the competition with other 'organic beings':

> On the confines of its geographical range, a change of constitution with respect to climate would clearly be an advantage to our plant; but we have reason to believe that only few plants or animals range so far, that they are destroyed exclusively by the rigour of the climate. Not until we reach the extreme confines of life, in the Artic regions or on the borders of an utter desert, will competition cease.
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> (Darwin, 1875, p. 60)

In environments that are generally rather stable and have a continuous high energy and biomass production, such as some tropical or marine environments, the above-cited view of Darwin may be a proper description of the forces that shape the distributional range and abundance of species. However, in temperate climates, where the environment is more variable and unpredictable, this may not be an appropriate description any more. There environmental stress may have a significant impact on the evolutionary and ecological processes that affect and shape the genetic structure and evolution of populations, as indicated by data obtained from natural populations during the 1940s and 1950s by *Drosophila* researchers like Timofeeff-Ressovsky and Dobzhansky. Their investigations have led to increased interest in studying the role of environmental stress in relation to natural selection for stress resistance and adaptation. After a brief period during the 1970s and 1980s when most interest was directed to neutral evolution (Kimura, 1983), evolutionary adaptation has been receiving increasingly more attention as is evinced by the publication of a number of monographs on these issues during the last decades (e.g. Calow & Berry, 1989; Hoffmann & Parsons, 1991, 1997; Bijlsma & Loeschcke, 1997). Especially in the light of the growing impact of human activities on natural environments, causing rapid and often stressful and deteriorating changes, research into stress responses and adaptation to stress is becoming an even more important and rapidly progressing field, not least because of the incorporation of new (gen-)omic techniques (Hoffmann *et al.*, 2003). The contributions appearing in this issue of JEB provide a good overview of the broad issues and approaches in current studies in environmental stress research. The papers collected here are the result of a 3-day workshop that was organized by us in August 2004 in Sandbjerg, Denmark.

Defining stress

Although the word 'stress' is well known to most biologists, it has proven to be a very elusive concept that is used in the scientific literature in many different ways and different contexts. This is not surprizing as one can have different perspectives on stress depending on the discipline (e.g. physiology, ecology and evolutionary biology), and biological level of interest (viz. molecular, physiological, organism or population level). Most importantly, however, stress is not only an attribute of the stressor (the environmental component), but also an attribute of the stressed (the biological component). For instance, whereas a polar bear would experience 25 °C as life threatening because it cannot dispose of its body heat and cooks itself to death when hunting, a Drosophila at the same temperature thrives near optimal. At temperatures below zero the roles naturally would be reversed. Therefore, environmental stress and the level of stress imposed can only be defined in relation to the organism or population experiencing this particular stress. In general, we expect organisms and populations to be the least stressed in the environment they experience most of the time, and to become increasingly stressed when they encounter environments, which are more alien to them. This implies that organisms and populations are expected to be better adapted to daily and seasonal changes in temperature that are encountered regularly than to more extreme temperatures that occur only sporadically. Although the term stress is most often used to indicate either the environmental or the biological component, it is clear that from an evolutionary perspective environmental pressure and biological response should be considered integrative. This implies at the same time that changes in level of stress experienced by organisms or populations can be a consequence of changes of either the stressor or the stressed.

Given the considerations above, it is not unexpected that stress has been defined in many different ways. Many definitions consider stress in a physiological context: the physiological responses of individuals to environmental stresses that affect their performance and well being. From the perspective of the contributions on stress related research in this issue, we are more concerned about defining stress in an evolutionary context. As pointed out above, stress should be considered both in relation to the stressor and the stressed, and therefore evolutionary definitions should incorporate both these aspects. Definitions of this type, for example, are:

An environmental condition that, when first applied, impairs Darwinian fitness (Sibly & Calow, 1989) any environmental change that acts to reduce the fitness of organisms (Koehn & Bayne 1989) stress is an environmental factor causing a change in the biological system which is potentially injurious. (Hoffmann & Parsons, 1991).

All these definitions emphasize a reduction in fitness of the organism or population caused by the environmental factor. To overcome such fitness reductions, organisms and populations can respond phenotypically or genetically and evolve adaptive mechanisms to reduce the detrimental impact of the stress. This is the kind of definitions that authors of the following contributions have had in mind when aiming to understand the impact of stress on the biological system and adaptive mechanisms that may be the result of this.

It should be noted that general definitions that define stress simply as 'a reduction in fitness' would mean that any reduction in fitness, whether small or large, would be regarded as stressful. As pointed out by Hoffmann & Parsons (1991) this would imply that in the wild most organisms and populations would experience stress all the time, as the environmental conditions would deviate from optimal most of the time and, consequently, maximum fitness is never attained. Many scientists, therefore, prefer the term stress to be applied when the intensity of the stress reaches levels that potentially limit survival or reproduction drastically, thereby endangering the existence of organisms and populations. However, as the intensity of stress often varies at a continuous scale, and in fact the intensity can often be judged only a posteriori, it is difficult to decide beyond what level of intensity it should be called stress rather than 'natural' variation of the environmental conditions.

Causation of stress

Environmental stress is considered to be primarily a response to physical features of the environment. Extrinsic stress that results from changes in abiotic factors such as temperature, climatic factors and chemical components, either naturally occurring or man-made, is regarded as the most important stress agent (Lindgren & Laurila, 2005; Sørensen et al., 2005). In addition, biotic stresses, such as competition, predation, and parasitism, can also cause stress (Relyea, 2005). Although abiotic and biotic stress can act independently, these two types of stress often act synergistically, as organisms that have suboptimal fitness because of abiotic stress often suffer more from predators and parasites. However, as pointed out before, environmental stress can only be valued in relation to the organism experiencing the stress, and therefore stress also has an intrinsic component. Genetic changes in organisms and populations brought about, for instance, by inbreeding or other changes in the genetic architecture of organisms or populations, can drastically change the perception of an otherwise unchanged (stress) environment, resulting in what is sometimes called 'genetic stress' (Bijlsma et al., 1997, 2000). Consequently, inbred populations may suffer greatly from changes in the environment that by noninbred populations would be perceived as nonstressful. This indicates that intrinsic and extrinsic stress may often strongly

interact, and there is increasing evidence that this leads to a strong synergism between the two stresses causing normally nonsevere stresses to become harmful when combined (Jiménez *et al.*, 1994; Bijlsma *et al.*, 2000; Keller *et al.*, 2002).

As the extrinsic and intrinsic causes of stress generally occur together in a nonadditive manner, they should preferably be investigated jointly. This is particularly important as the growing human population causes major changes in the biotic and abiotic environment at an unprecedented scale and a fast rate. Global warming causing thermal stress and pollution exerting chemical stress go hand in hand with destruction and fragmentation of natural habitats. As the latter will inevitably go together with smaller and more isolated populations that become subject to genetic erosion, many populations and organisms will simultaneously experience deteriorating environmental conditions and genetic stress (Frankham, 2005). Therefore, understanding the nature, interactions and consequences of these stresses at a global scale from an ecological and evolutionary perspective is of the utmost importance, not only to understand the processes involved, but also to develop and evaluate possible countermeasures.

Adaptation and evolution

Like stress, adaptation is also a concept that often causes confusion as it is used in many different ways and contexts, and many definitions are simply physiologically oriented and less suitable in an evolutionary context. In a general sense, adaptation can be defined as the process of change in an organism to conform better with (new) environmental conditions, whereby the organism (or group of organisms) acquires characteristics, involving changes in morphology, physiology or behaviour, that improve their survival and reproductive success in the particular environment. Such changes can occur phenotypically, within a set genotype, and then *phenotypic adaptation* is the result of what is called 'phenotypic plasticity', the capability of a genotype to change its phenotype according to prevailing environmental conditions. Morphological changes and other inducible defences as modelled or described for tadpoles and *Daphnia* in response to the presence of predators fall within this category (Gabriel, 2005; Pauwels *et al.*, 2005; Relyea, 2005), but also maternal effects in a parthenogenetic strain of *Drosophila mercatorum* (Andersen *et al.*, 2005). Adaptation can also occur through changes in allele frequencies as a result of the selection pressure exerted by the environment (e.g. David *et al.*, 2005; Lindgren & Laurila, 2005; Sørensen *et al.*, 2005). This process is known as *genotypic adaptation* or *evolutionary adaptation*. As the occurrence of plasticity and possibly also the degree of plasticity are genetically based, both these phenomena are important from an evolutionary perspective.

Adaptive traits may also be the result of correlated responses, in that selection is not directly acting on the trait of study (Bubliy & Loeschcke, 2005; Hoffmann *et al.*, 2005; Malherbe *et al.*, 2005). A better understanding of genetic correlations and trade-offs in a stress scenario can be achieved by artificial selection experiments. However, it is important to note that at least some if not most of the correlated responses and/or trade-offs may be genotype (population) and/or environment specific.

Although the occurrence of the adaptive process in evolution is well documented and also clearly shown by the fact that many organisms have adapted quite rapidly to man-made changes in the environment (e.g. pollution, pesticides, thermal stress; Bradshaw, 1952; Woods, 1981; Macnair, 1997; Hoffmann *et al.*, 2003), we still know little about the dynamics of the adaptive process, and several models are still to be explored and tested. Already in the 1930s, during the foundation of population genetics theory, controversy arose about the mode of genetic and adaptive changes underlying evolution. According to Fisher, evolution proceeded at the genetic level mainly by largely independent allele substitutions at many loci, each having little effect on fitness (Fisher, 1930). Wright, on the other hand, argued, that populations often are characterized by 'co-adapted' combinations of alleles at interacting loci (Wright, 1931). The question is clearly of great fundamental importance, since in Wright's view the genetic structure of populations may constrain evolutionary changes because natural selection will often be unable to carry a population through an adaptive valley, and the valley can only be crossed 'by chance', i.e. through genetic drift. The importance of Wright's view is that it would explain the occurrence of phenomena like (negative) epistatic interactions, the cost of resistance and compensatory evolution, and possibly partly inbreeding depression. In Fisher's view, natural selection will essentially always be able to improve the adaptedness of populations, provided sufficient genetic variation is present. This controversy has never been fully resolved, and today population geneticists are still divided in their opinions on this matter (e.g. Coyne *et al.*, 1997; Wade & Goodenough, 1998). Clearly, much more research is needed even to begin to understand the dynamics of adaptation and its consequences for the evolutionary process. However, when populations are small and the evolutionary potential for adaptive evolution in the Fisherian sense becomes limited anyhow, chance will play a crucial role for further persistence of a population, whether it can track environmental change or will become extinct.

The possible occurrence of evolutionary adaptation and the rate at which it can proceed depends on the presence and the fitness effects of the mutations involved (de Visser & Rozen, 2005). The initial response to changing conditions predominantly depends on the level of standing genetic variation. It is not clear at the moment how limited this amount of adaptive variation

is in natural populations. Quantitative models from artificial selection experiments (Kristensen *et al.*, 2005) and the rapid response of many organisms to pesticide treatments suggest that there is ample standing genetic variation available for most traits in most populations for evolutionary response. However, we have little information at the moment on whether this level of variation is sufficient to facilitate long-term adaptive processes, or that in the long run evolution and adaptation largely depend on fixation of new beneficial mutations. Experimental evolution experiments with bacteria seem to suggest that mutation rates are a limiting factor in long-term evolution processes (de Visser & Rozen, 2005). As to the size of the fitness effects of beneficial mutations, little is currently known: Evolution of pesticide resistance often suggests that a few genes with large effects are involved, whereas quantitative genetic experiments suggest that many characters are governed by many genes, each with a small effect. Investigating these aspects in the near future using experimental evolution and model organisms is of the utmost importance to begin to understand the evolutionary adaptive process (Schoustra *et al.*, 2005).

Assuming that the initial short-term response of organisms depends largely on the standing genetic variation within populations is of great significance for disturbed ecosystems where nature has become highly fragmented. In fragmented landscapes, populations are generally small and relatively isolated and therefore increasingly subject to genetic drift (and inbreeding), thereby depleting standing genetic variation. Consequently, such genetically eroded populations are expected to have a lower evolutionary potential than nonfragmented populations (Kristensen *et al.*, 2005). In addition to the observation that inbred populations are often much more sensitive to environmental stress (see above) this indicates that research into the dynamics of stress adaptation should also be an integral part of conservation biology (Frankham, 2005; Pedersen *et al.*, 2005).

Environmental stress and contributions of this issue

In our opinion, the contributions on environmental stress appearing in this issue of the Journal of Evolutionary Biology represent a broad cross-section of the current state of the art in evolutionary research in environmental stress, with particular focus on a few specific topics. Several papers are concerned with the role of inbreeding and the rate of inbreeding for fitness and evolutionary potential with clear-cut implications for conservation biology (Frankham, 2005; Kristensen *et al.*, 2005; Pedersen *et al.*, 2005). Experimental evolution with rapidly growing and reproducing organisms has recently been used successfully to test some basic issues of evolutionary adaptation, such as on the rate of compensatory evolution and adaptation (de Visser & Rozen, 2005; Schoustra *et al.*,

2005). Artificial selection experiments for stress resistance are used to test for correlated responses and trade-offs (Bubliy & Loeschcke, 2005; Hoffmann *et al.*, 2005) and to address functional relationships among traits (Malherbe *et al.*, 2005). Thermal adaptation along climatic gradients is the topic of another set of papers studying variation in life history traits along latitudinal and altitudinal gradients (David *et al.*, 2005; Gomez-Mestre & Tejedo, 2005; Lindgren & Laurila, 2005; Sørensen *et al.*, 2005). Predator induced defences; phenotypic plasticity and maternal effects are the focus of another set of papers (Andersen *et al.*, 2005; Gabriel, 2005; Pauwels *et al.*, 2005; Relyea, 2005). Finally, the role for environment-dependent selection on speciation (Lexer & Fay, 2005) and the biological limitations of transcriptomics in studies of stress responses and their evolution (Feder & Walser, 2005) are discussed.

Progress and future of stress research

Since we edited the 1997 volume on Environmental Stress, Adaptation and Evolution (Bijlsma & Loeschcke, 1997), the field has moved from a more descriptive to a more analytical level. Hypotheses have become more precise and targeted at functional relationships (e.g. Malherbe *et al.*, 2005). Molecular techniques are an integrative part of many studies and their application will become even more important in the years to come. Statistical methods to analyse the stress response now include Bayesian approaches (e.g. Kristensen *et al.*, 2005), adaptive responses to stress are modelled by experimental evolution (e.g. de Visser & Rozen, 2005; Schoustra *et al.*, 2005), the importance of genotype × environment interactions (Bubliy & Loeschcke, 2005) has become widely accepted, evidence on the strong pattern of thermal adaptation has accumulated (Sørensen *et al.*, 2005) and quantitative genetic techniques and estimators are now commonly applied in the stress literature (e.g. Kristensen *et al.*, 2005; Relyea, 2005). The importance of stress research for conservation biology has become obvious (Frankham, 2005).

In the years to come we will see further incorporation of genomics and other omics techniques into the research on the stress response and its evolution, with the aim of identifying and analysing genes that matter and interactions involved (Loeschcke *et al.*, 2004). Given that each specific omics approach gives only part of the answer, we need an integrative approach incorporating: (1) selection lines, (2) genetic correlations and trade-offs, (3) the quantitative genetics of the traits under study, (4) the role of genotype-by-environment interactions, (5) QTL analysis, (6) candidate gene approach, with (7) transcriptomics, proteomics and metabonomics and (8) investigation of the presence of the revealed variation in candidate genes in natural populations for understanding the proximate and ultimate processes/factors involved in stress resistance and adaptation. In our view

such an integrative approach is needed to fully understand the impact of stress on the evolution and persistence of biological systems.

Acknowledgments

References

Andersen, D.H., Pertoldi, C., Scali, V. & Loeschcke, V. 2005. Heat stress and age induced maternal effects on wing size and shape in parthenogenetic *Drosophila mercatorum*. *J. Evol. Biol.* **18**: 884–892.

Bijlsma, R., Bundgaard, J., Boerema, A.C. & Van Putten, W.F. 1997. Genetic and environmental stress, and the persistence of population. In: *Environmental Stress, Adaptation and Evolution* (R. Bijlsma & V. Loeschcke, eds), pp. 193–207. Birkhäuser Verlag, Basel, CH.

Bijlsma, R., Bundgaard, J. & Boerema, A.C. 2000. Does inbreeding affect the extinction risk of small populations? Predictions from *Drosophila*. *J. Evol. Biol.* **13**: 502–514.

Bijlsma, R. & Loeschcke, V. (eds) 1997. *Environmental Stress, Adaptation and Evolution*. Birkhäuser Verlag, Basel, CH.

Bradshaw, A.D. 1952. Populations of *Agrostris tenuis* resistant to lead and zink poisoning. *Nature* **169**: 1098.

Bubliy, O.A. & Loeschcke, V. 2005. Correlated responses for stress resistance and longevity in a laboratory population of *Drosophila melanogaster*. *J. Evol. Biol.* **18**: 789–803.

Calow, P. & Berry, R.J. 1989. *Evolution, Ecology and Environmental Stress*. Academic Press, London, UK.

Coyne, J., Barton, N. & Turelli, M. 1997. A critique of the shifting balance theory of evolution. *Evolution* **51**: 643–671.

Darwin, C. 1875. *The Origin of Species by means of Natural Selection*, 6th edn. Murray, London, UK.

David, J.R., Araripe, L.O., Chakir, M., Legout, H., Lemos, B., Petavy, G., Rohmer, C., Joly, D. & Moreteau, B. 2005. Male sterility at extreme temperatures: a significant but neglected phenomenon for understanding *Drosophila* climatic adaptations. *J. Evol. Biol.* **18**: 838–846.

de Visser, J.A.G.M. & Rozen, D.E. 2005. Limits to adaptation in asexual populations. *J. Evol. Biol.* **18**: 779–788.

Feder, M.E. & Walser, J.-C. 2005. The biological limitations of transcriptomics in elucidating stress and stress responses. *J. Evol. Biol.* **18**: 901–910.

Fisher, R.A. 1930. *The Genetical Theory of Natural Selection*. Clarendon Press, Oxford, UK.

Frankham, R. 2005. Stress and adaptation in conservation genetics. *J. Evol. Biol.* **18**: 750–755.

Gabriel, W. 2005. How stress selects for reversible phenotypic plasticity. *J. Evol. Biol.* **18**: 873–883.

Gomez-Mestre, I. & Tejedo, M. 2005. Adaptation or exaptation? An experimental test of hypotheses on the origin of salinity tolerance in *Bufo calamita*. *J. Evol. Biol.* **18**: 847–855.

Hoffmann, A.A. & Parsons, P.A. 1991. *Evolutionary Genetics and Environmental Stress*. Oxford University Press, Oxford, UK.

Hoffmann, A.A. & Parsons, P.A. 1997. *Extreme Environmental Change and Evolution*. Cambridge University Press, Cambridge, UK.

Hoffmann, A.A., Hallas, R., Anderson, A.R. & Telonis-Scott, M. 2005. Evidence for a robust sex-specific trade-off between cold resistance and starvation resistance in *Drosophila melanogaster*. *J. Evol. Biol.* **18**: 804–810.

Hoffmann, A.A., Sørensen J.G. & Loeschcke, V. 2003. Adaptation to extreme temperatures in *Drosophila* combining quantitative and molecular approaches. *J. Therm. Biol.* **28**: 175–216.

Jiménez, J.A., Hughes, K.A., Alaks, G., Graham, L. & Lacy, R.C. 1994. An experimental study of inbreeding depression in a natural habitat. *Science* **266**: 271–273.

Keller, L.F., Grant, P.R., Grant, B.R. & Petren, K. 2002. Environmental conditions affect the magnitude of inbreeding depression in survival of Darwin's finches. *Evolution* **56**: 1229–1239.

Kimura, M. 1983. *The Neutral Theory of Evolution*. Cambridge University Press, Cambridge, UK.

Koehn, R.K. & Bayne, R.L. 1989. Towards a physiological and genetical understanding of the energetics of the stress response. *Biol. J. Linn. Soc.* **37**: 157–171.

Kristensen, T.N., Sørensen, A.C., Sorensen, D., Pedersen, K.S., Sørensen, J.G. & Loeschcke, V. 2005. A test of quantitative genetic theory using *Drosophila* – effects of inbreeding and rate of inbreeding on heritabilities and variance components. *J. Evol. Biol.* **18**: 763–770.

Lexer, C. & Fay, M.F. 2005. Adaptation to environmental stress: a rare or frequent driver of speciation? *J. Evol. Biol.* **18**: 893–900.

Lindgren, B. & Laurila, A. 2005. Proximate causes of adaptive growth rates: growth efficiency variation among latitudinal populations of *Rana temporaria*. *J. Evol. Biol.* **18**: 820–828.

Loeschcke, V., Sørensen, J.G. & Kristensen, T.N. 2004. Ecologically relevant stress resistance: from microarrays and QTL to candidate genes – a research plan and preliminary results using *Drosophila* as a model organism and climatic and genetic stress as model stresses. *J. Biosci.* **29**: 101–109.

Macnair, M.R. 1997. The evolution of plants in metal-contaminated environments. In: *Environmental Stress, Adaptation and Evolution* (R. Bijlsma & V. Loeschcke, eds), pp. 3–24. Birkhäuser Verlag, Basel, CH.

Malherbe, Y., Kamping, A., van Delden, W. & de Zande, L. 2005. ADH enzyme activity and *Adh* gene expression in *Drosophila melanogaster* lines differentially selected for increased alcohol tolerance. *J. Evol. Biol.* **18**: 811–819.

Pauwels, K., Stoks, R. & de Meester, L. 2005. Coping with predator stress: interclonal differences in induction of heat shock proteins in the water flea *Daphnia magna*. *J. Evol. Biol.* **18**: 867–872.

Pedersen, K.S., Kristensen, T.N. & Loeschcke, V. 2005. Effects of inbreeding and rate of inbreeding in *Drosophila melanogaster* – Hsp70 expression and fitness. *J. Evol. Biol.* **18**: 756–762.

Relyea, R.A. 2005. The heritability of inducible defences in tadpoles. *J. Evol. Biol.* **18**: 856–866.

Schoustra, S.E., Slakhorst, M., Debets, A.J.M. & Hoekstra, R.F. 2005. Comparing artificial and natural selection in rate of adaptation to genetic stress in *Aspergillus nidulans*. *J. Evol. Biol.* **18**: 771–778.

Sibly, R.M. & Calow, P. 1989. A life cycle theory of responses to stress. *Biol. J. Linn. Soc.* **37**: 101–116.

Sørensen, J.G., Norry, F.M., Scannapieco, A.C. & Loeschcke, V. 2005. Altitudinal variation for stress resistance traits and thermal adaptation in adult *Drosophila buzzatii* from the New World. *J. Evol. Biol.* **18**: 829–837.

Wade, M. & Goodenough, C. 1998. The theories of Fisher and Wright in the context of metapopulations: when nature does many small experiments. *Evolution* **52**: 1537–1553.

Woods, R.J. 1981. Insecticide resistance: genes and mechanisms. In: *Genetic Consequences of Man Made Change* (J. A. Bishop & L. M. Cook, eds), pp. 53–96. Academic Press, London, UK.

Wright, S. 1931. Evolution in Mendelian populations. *Genetics* **16**: 97–159.